Applicant: Gage et al. Attorney's Docket No.: 17136-002RE1

Serial No.: 09/269,278 Filed: June 30, 1999

Page : 2 of 6

AMENDMENTS TO THE CLAIMS

Please make the following changes to the claims:

1. (amended): A screening method for determining ion channel modulating activity of a test substance having potential for such modulating activity, which comprises the steps of:

- (i) contacting a host cell with the test substance, said host cell expressing a peptide, polypeptide or protein in the plasma membrane[of a host cell], said peptide, polypeptide or protein having ion channel activity when expressed as a heterologous protein in the plasma membrane of the host cell; and
- [(ii) contacting said host cell with the test substance; and]
- [(iii)](ii) determining changes to the ion channel activity of said heterologous protein induced by the test substance, wherein the changes to the ion channel activity of the heterologous protein induced by the test substance are determined by detecting the effect of the test substance on changes in net movement across the plasma membrane of the host cell of small cellular metabolite molecules which do not directly permeate the ion channel formed by said heterologous protein.
- 9. (amended): A method for determining ion channel modulating activity of a test substance having potential for such modulating activity, which comprises the steps of:

Applicant: Gage et al. Attorney's Docket No.: 17136-002RE1

Serial No.: 09/269,278 Filed: June 30, 1999

Page : 3 of 6

(i) contacting a host cell with the test substance, said host cell expressing a peptide, polypeptide or protein in the plasma membrane[of a host cell], said peptide, polypeptide or protein having ion channel activity when expressed as a heterologous protein in the

[(ii) contacting said host cell with the test substance; and]

plasma membrane of the host cell; and

- [(iii)](ii) determining changes to the ion channel activity of said heterologous protein induced by the test substance, wherein the changes to the ion channel activity of the heterologous protein induced by the test substance are determined by detecting the effect of the test substance on changes in permeability of the plasma membrane of the host cell to small cellular metabolite molecules, wherein said heterologous protein having ion channel activity is the HIV-1 Vpu integral membrane protein.
- 14. (amended): A screening method for determining ion channel modulating activity of a test substance having potential for such modulating activity, which comprises the steps of:
 - (i) contacting a host cell with the test substance, said host cell expressing HIV-1 Vpu integral membrane protein in the plasma membrane of a host cell, said protein having ion channel activity when expressed as a heterologous protein in the plasma membrane of the host cell; and
 - [(ii) contacting said host cell with the test substance; and]
 - [(iii)](ii) determining changes to the ion channel activity of said heterologous protein induced by the test substance, wherein the changes to the ion channel activity of

Applicant: Gage et al. Attorney's Docket No.: 17136-002RE1

Serial No.: 09/269,278 Filed: June 30, 1999

Page : 4 of 6

the heterologous protein induced by the test substance are determined by detecting the effect of the test substance on changes in net movement across the plasma membrane of the host cell of small cellular metabolite molecules.

19. (amended): A screening method for determining ion channel modulating activity of a test substance having potential for such modulating activity, which comprises the steps of:

- (i) contacting a host cell with the test substance, said host cell expressing HIV-1 Vpu integral membrane protein in the plasma membrane[of a host cell], said protein having ion channel activity when expressed as a heterologous protein in the plasma membrane of the host cell; and
- [(ii) contacting said host cell with the test substance; and]
- [(iii)](ii) determining changes to the ion channel activity of said heterologous protein induced by the test substance.